Stroke

BRIEF REPORT

Acute Ischemic Stroke in Patients With COVID-19

An Analysis From Get With The Guidelines–Stroke

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BACKGROUND AND PURPOSE: Studies suggest an increased risk of adverse outcomes among patients with acute ischemic stroke (AIS) and coronavirus disease 2019 (COVID-19).

METHODS: Using Get With The Guidelines–Stroke, we identified 41 971 patients (AIS/COVID-19: 1143; AIS/no COVID-19: 40 828) with AIS hospitalized between February 4, 2020 and June 29, 2020, from 458 Get With The Guidelines–Stroke hospitals with at least one COVID-19 case and evaluated clinical characteristics, treatment patterns, and outcomes.

RESULTS: Compared with patients with AIS/no COVID-19, those with AIS/COVID-19 were younger, more likely to be non-Hispanic Black, Hispanic, or Asian, more likely to present with higher National Institutes of Health Stroke Scale scores, and had greater proportions of large vessel occlusions. Rates of thrombolysis and thrombectomy were similar between the groups. Door to computed tomography (median 55 [18–207] versus 35 [14–99] minutes, $P<0.001$), door to needle (59 [40–82] versus 46 [33–64] minutes, $P<0.001$), and door to endovascular therapy (114 [74–169] versus 90 [54–133] minutes, $P=0.002$) times were longer in the AIS/COVID-19 cohort. In adjusted models, patients with AIS/COVID-19 had decreased odds of discharge with modified Rankin Scale score of ≤2 (odds ratio, 0.65 [95% CI, 0.52–0.81], $P<0.001$) and increased odds of in-hospital mortality (odds ratio, 4.34 [95% CI, 3.48–5.40], $P<0.001$).

CONCLUSIONS: This analysis demonstrates younger age, greater stroke severity, longer times to evaluation and treatment, and worse morbidity and mortality in patients with AIS/COVID-19 compared with those with AIS/no COVID-19.

GRAPHIC ABSTRACT: An online graphic abstract is available for this article.

Key Words: coronavirus ■ COVID-19 ■ hospital ■ ischemic stroke ■ mortality

Prior cohorts demonstrate poor outcomes in patients with coronavirus disease 2019 (COVID-19) and acute ischemic stroke (AIS).[1,2] Using data from Get With The Guidelines–Stroke (GWTG–Stroke), we investigate the characteristics, diagnostics, and outcomes of patients with AIS and COVID-19 in the United States.

METHODS

GWTG–Stroke is a national stroke registry/quality improvement program implemented in over 2000 United States hospitals. Patients were enrolled without consent through the Common Rule or through an institutional review board authorization/exemption waiver. Data collection and analysis were performed by IQVIA, Inc (Parsippany, New Jersey) and Duke Clinical Research Institute,

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Nonstandard Abbreviations and Acronyms

AIS	acute ischemic stroke
COVID-19	coronavirus disease 2019
GWTG–Stroke	Get With The Guidelines–Stroke

respectively. This study was approved by the Duke University Institutional Review Board. Given that data were collected for clinical care and quality improvement, rather than primarily for research, data sharing agreements require an application process for other researchers to access the data. Interested researchers can submit proposals to utilize GWTG for research purposes, including for validation purposes. Proposals can be submitted at www.heart.org/qualityresearch. Additional information regarding the statistical analysis plan and analytic code may also be available from Duke Clinical Research Institute upon request.

The study population consisted of 41 971 (AIS/COVID-19: 1143; AIS/no COVID-19: 40 828) patients with AIS hospitalized between February 4, 2020 and June 29, 2020, from 458 GWTG–Stroke hospitals with at least one recorded COVID-19 case (Figure I in the Data Supplement). Statistical methods are detailed in the Methods in the Data Supplement. Variable missingness is shown in Table I in the Data Supplement.

RESULTS

The study population consisted of 41 971 patients with AIS, of whom 1143 had a diagnosis of COVID-19. Patients with AIS/COVID-19 were younger, more likely to be Hispanic, non-Hispanic Black, or Asian, and more likely to be Medicaid or self-pay/no insurance than patients with AIS/no COVID-19. Patients with AIS/COVID-19 had higher National Institutes of Health Stroke Scale scores, more large vessel occlusions, and were found to present more frequently via emergency medical services (Table; Table II in the Data Supplement).

Rates of thrombolysis and endovascular therapy were similar between the two groups. Door to computed tomography (median 55 [18–207] versus 35 [14–99] minutes, $P<0.001$), door to needle (58.5 [40–82] versus 46 [33–64] minutes, $P<0.001$), and door to endovascular therapy (114 [74–169] versus 90 [54–133] minutes, $P=0.002$) times were significantly longer in the AIS/COVID-19 group (Table III in the Data Supplement). Treatment delay reasons are shown in Table IV in the Data Supplement. GWTG–Stroke achievement/quality measures are shown in Table V in the Data Supplement. In adjusted logistic regression models, patients with AIS/COVID-19 (compared with AIS/no COVID-19) had increased odds of inpatient mortality (odds ratio, 4.34 [95% CI, 3.48–5.40], $P<0.001$), and decreased odds of discharge with modified Rankin Scale score of ≤2 (odds ratio, 0.65 [95% CI, 0.52–0.81], $P<0.001$) (Table VI in the Data Supplement). In adjusted models, prior anticoagulant use, stroke severity, and arrival via emergency medical services positively associated with odds of in-hospital mortality among patients with AIS/COVID-19 (Table VII in the Data Supplement).

DISCUSSION

In one of the largest and most geographically diverse studies of patients with AIS/COVID-19 to date, we describe the clinical characteristics, treatment patterns, and outcomes of patients with AIS/COVID-19.

Similar to prior studies, we demonstrate increased morbidity/mortality among patients with AIS/COVID-19.[1–3] COVID-19 affects nearly every organ system, which places patients with the virus at increased risk of adverse outcomes.[4] Although we are able to control for baseline patient characteristics, we are unable to account for COVID-19 severity due to the nature of GWTG–Stroke, limiting our ability to determine what proportion of the observed increase in adverse outcomes is being driven by COVID-19 severity, and its effect on other organ systems.

From a neurological perspective, patients with AIS/COVID-19 presented with higher National Institutes of Health Stroke Scale scores, and a greater proportion of large vessel occlusion strokes. They were also found to more frequently present by emergency medical services, further suggesting increased stroke severity. Prior research demonstrates a positive correlation between increasing National Institutes of Health Stroke Scale scores and 30-day mortality, as well as increased rates of mortality after large vessel occlusion ischemic strokes.[5,6] Indeed, we demonstrate that arrival via emergency medical services and increasing National Institutes of Health Stroke Scale scores associate with odds of inpatient mortality among those with AIS/COVID-19. These findings are consistent with prior work in this population.[1,3] Increased stroke severity may be explained by a combination of COVID-19–associated increases in stroke severity and the hypothesis that patients with COVID-19 and mild stroke symptoms may be staying home at greater rates due to the pandemic.

Patients with AIS/COVID-19 were treated with thrombolytics and endovascular therapy at rates similar to patients with AIS/no COVID-19. However, patients with AIS/COVID-19 were found to have longer door to computed tomography, door to needle, and door to endovascular times compared with patients without COVID-19. Imaging and procedural interventions of patients with COVID-19 have been challenging during the pandemic due to required protocols for protection of health care workers.[7] Similar to our findings, prior studies have also demonstrated delays in door to diagnosis and door to intervention times, and subsequent increases in mortality, among patients with AIS/COVID-19.[1,8]

Patients with AIS/COVID-19 were more frequently non-Hispanic Black, Hispanic, and Asian, and more likely to have Medicaid/self-pay/no insurance compared with those with AIS/no COVID-19. Similar disparities in care have been observed by others, and are likely a reflection of long-standing systemic social inequities.[9]

Table. Characteristics of the Cohort of Acute Ischemic Stroke Patients Stratified by COVID-19 Status

	Overall	With COVID-19	Without COVID-19	
	N=41 971	N=1143	N=40 828	*P* value*
Demographics				
Age, y	71 (60–81)	68 (57–79)	71 (60–81)	<0.001
Female, n (%)	20 406 (48.6)	528 (46.2)	19 878 (48.7)	0.10
Race, n (%)				<0.001
Asian	1313 (3.1)	56 (4.9)	1257 (3.1)	
Non-Hispanic Black	9372 (22.3)	357 (31.3)	9015 (22.1)	
Hispanic	3226 (7.7)	178 (15.6)	3048 (7.5)	
Non-Hispanic White	25 857 (61.6)	441 (38.6)	25 416 (62.3)	
Other	2183 (5.2)	110 (9.6)	2073 (5.1)	
Insurance, n (%)				<0.001
Self-pay/no insurance	1732 (4.1)	51 (4.5)	1681 (4.1)	
Medicare	15 635 (37.3)	339 (29.7)	15 296 (37.5)	
Medicaid	5492 (13.1)	238 (20.8)	5254 (12.9)	
Private/veterans affairs/CHAMPUS/other	13 590 (32.4)	376 (32.9)	13 214 (32.4)	
Not documented	5522 (13.2)	139 (12.2)	5383 (13.2)	
Medical comorbidities, n (%)				
Atrial fibrillation/flutter	7456 (17.8)	190 (16.6)	7266 (17.8)	0.31
Coronary artery disease	9150 (21.8)	224 (19.6)	8926 (21.9)	0.07
Diabetes	14 965 (35.7)	502 (43.9)	14 463 (35.4)	<0.001
Heart failure	4351 (10.4)	131 (11.5)	4220 (10.3)	0.22
Hypertension	31 876 (76.0)	815 (71.3)	31 061 (76.1)	<0.001
Peripheral vascular disease	1696 (4.0)	52 (4.6)	1644 (4.0)	0.38
Previous stroke	10 547 (25.1)	244 (21.4)	10 303 (25.2)	0.003
Previous transient ischemic attack	3192 (7.6)	54 (4.7)	3138 (7.7)	<0.001
Serum creatinine > 2 mg/dl	4767 (11.4)	137 (12.0)	4630 (11.3)	0.50
Clinical characteristics				
NIH Stroke Scale	4 (1–10)	8 (3–17)	4 (1–9)	<0.001
Large vessel occlusion stroke, n (%)	9047 (23.8)	307 (30.4)	8740 (23.6)	<0.001
Time from symptom onset to arrival, min†	322 (103–815)	313 (94–755)	323 (103–817)	0.19

CHAMPUS indicates Civilian Health and Medical Program of the Uniformed Services; COVID-19, coronavirus disease 2019; and NIH, National Institutes of Health.

*Continuous variables presented as median (25th–75th percentile).

†Symptom onset defined as last known well time.

GWTG–Stroke data were collected retrospectively, allowing for the evaluation of associations but not causation. Although regression models were adjusted for confounders, the risk for unmeasured confounding remains. Details on the characteristics, severity, or treatments of patients with COVID-19 were not available. Data reflect care patterns and outcomes during the earlier phases of the pandemic.

CONCLUSIONS

In this analysis of 41 971 patients, we demonstrate greater stroke severity, similar acute treatment use but less timely stroke care, and worse outcomes in patients presenting with AIS/COVID-19. These findings suggest the need for investigation into enhanced protocols and interventions to improve the timely care of those presenting with AIS and COVID-19 during the pandemic.

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